00005.001217.PC PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Deirdre Renee Claytor
HIROSHI KASE, ET AL.	)	
	:	Group Art Unit: 1627
Application No.: 10/553,250	)	
	:	Confirmation No. 6976
Filed: October 17, 2005	)	
	:	
For: A METHOD OF TREATING AN ANXIETY DISORDER	)	
	:	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

I, Tomoyuki Kanda, Ph.D., do hereby declare as follows:

1. I attended Toyama Medical and Pharmaceutical University from 1985-1988 and received a Bachelors in Pharmacology in 1988.

2. From 1988-1990, I attended Graduate School of Pharmacology at Osaka University and received a Masters of Science in Pharmacology in 1990. I received my Ph.D. in Pharmacology in 1999.

3. I have been employed by Kyowa Hakko Kogyo Co., Ltd. (now Kyowa Hakko Kirin Co., Ltd.) since 1990. My positions there have been:

1990-2003	Researcher in Neuropharmacology
1993-1995	Visiting Research Fellow of the King's College London, University of London
2003-2008	Senior Researcher, Pharmacological Research Laboratories Pharmaceutical Research Center
2008-present	Senior Scientist, Pharmacological Research Laboratories Research Division

4. I have nearly 25 years experience in pharmacology, and more than 19 years experience conducting pharmacological research and development, including specializing in the field of treating depression.

5. I am familiar with the prosecution of this application, including both the Examiner's rejection of the claims over the prior art and the Examiner's objections to Applicants' comparisons of compounds to "vehicle" for determining efficacy.

6. It is entirely conventional in the pharmaceutical art, when comparing the results of test runs (for evaluating the effects of drugs), to standardize each result to the vehicle value. That is, efficacy is normally presented as percent improvement over vehicle.

7. This is seen, for instance, in Shiozaki et al., Actions of adenosine A_{2A} receptor antagonist KW-6002 on drug-induced catalepsy and hypokinesia caused by reserpine or MPTP, *Psychopharmacology*, Vol. 147 (1999) 90-5, copy attached. Therein, the effects on locomotor counts are evaluated by standardization with the vehicle-treated (normal) group. See p. 93 right column, lines 3-20 and Fig. 3.

8. It is desired to standardize data with the vehicle value to compare the effects of drugs among different test runs, especially if the vehicle value is different among the test runs. Moreover, it should be understood that if compounds were not compared to vehicle,

then direct comparisons would needlessly have to be made anew every time a new compound was evaluated.

9. As to the present invention, test example 1 shows Istradefylline at 3 mg/kg po exhibited vastly more potent activity on the change of the number of head-dips than Compound C[1] at 10 mg/kg po. (Compare Table 1-A at page 50 with Table 1-C at page 51). Similarly, test examples 4 and 6 show the effects of Istradefylline on the Elevated Plus-Maze and Social Interaction tests are vastly more potent than those of Compound C. (Compare Table 3-A at page 55 with Table 3-C at page 56, and compare Table 4-A at page 56 with compare Table 4-C at page 57).

10. Compound C is a compound having Greenlee's triazolopyrimidine skeleton. Therefore, the record conclusively establishes the superiority of Istradefylline over the prior art for treating generalized anxiety disorder (claims 23 and 71), obsessive-compulsive disorder (claim 73), panic disorder (claim 75), agoraphobia (claim 77), and social phobia (claim 79).

11. From the foregoing, Applicants conclusively established that Istradefylline is unexpectedly superior over adenosine A_{2A} receptor antagonists that are structurally similar to those taught in the Examiner's prior art.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of

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[1] 5-amino-2-(2-furyl)-7-[4-(3-hydroxy-3-methylbutyl)piperazinyl][1,2,4]traizolo[1,5-c]pyrimidine, see page 40.

Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Tomoyuki Kanda, Ph.D.

Date: 31st Jul. 2010